REMARKS/ARGUMENTS:

Claims 1, 30, and 53 are amended. Support for the amendments to claims 1, 30, and 53 can be found at page 14, lines 13-26 of the Applicant's specification. Claims 1-32 and 34-72 are pending in the application. Reexamination and reconsideration of the application, as amended, are respectfully requested.

CLAIM REJECTIONS UNDER 35 U.S.C. §103:

Claims 1, 3, 7, 9, 11-14, 17-18, 22-28, 53, 55-58, 62, and 66-71 stand rejected under 35 U.S.C. §103(a) as being obvious over Jahn et al., *Proceedings of the National Academy of Sciences, USA*, (1984), Vol. 81, pages 1684-1687 ("Jahn") in view of Schermer et al. (U.S. Patent No. 6,485,918 B1) ("Schermer"). The Applicant respectfully traverses this rejection.

Claim 1, as amended, is as follows:

> A method for detecting a target biopolymer in a sample, comprising:
>
> (a) preparing a microarray of said sample by dispensing aliquots of said sample at discrete sites onto a substrate and immobilizing said target biopolymer on said substrate, wherein the microarray is an array of dots, each dot having a diameter from about 1 to 500 microns, wherein each of said aliquots contains the same amount of said target biopolymer;
>
> (b) contacting said microarray with a probe biopolymer under conditions that allow the formation of a complex comprising said target biopolymer and said probe biopolymer, wherein said probe biopolymer is applied to dots individually in said microarray; and
>
> (c) detecting the presence of said complex as a measurement for the presence or the amount of the target biopolymer in said sample.

Applicant respectfully submits that the cited references cannot render claim 1 obvious, because the cited references fail to teach or suggest that the probe biopolymer is applied to dots individually in the microarray. Unlike the present invention, Jahn does not utilize a microarray format. Jahn discloses a conventional dot-immunobinding assay of proteins in which a large number of different samples are spotted on nitrocellulose membrane filters, incubated sequentially with specific antibodies and $^{125}$I-labeled protein A, and assayed for radioactivity. (Jahn, Abstract). In Jahn, the entire membrane is incubated with specific antibodies and protein A. (Jahn, page 1684, column 2, line 43-page 1685, column, 1, line 8). Thus, in Jahn, the antibodies and protein A are not applied to dots individually but rather to the entire membrane.

Schermer cannot remedy the defect of Jahn. In Schermer, the liquid reagent is applied to the entire microarray and not to the dots individually within the microarray. Schermer states,

> "In operation, a volume of liquid reagent 56 is placed in the cover 50, and a microarray substrate 10 is placed on top of the liquid reagent-filled cover 50 with the top surface 12 (having spotted area 7) of the substrate 10 facing downward, toward the cover 50." (Schermer, column 5, lines 31-35).

Consequently, in Schermer, the microarray comprising all of the dots is applied to the liquid reagent. Therefore, neither Jahn nor Schermer offer the advantage of the present invention which is that each element (aliquot) of the array can be contacted with a different probe. (Applicant's specification, at page 14, lines 15-16). That is, the first element of the microarray is contacted with a first known probe, the second element of the microarray is contacted with a second known probe, etc., wherein the first, second, etc. probes may be the same or different. For example, the sample microarray could be contacted with one probe, or with four probes, each having a different, distinguishable label etc. since the composition of

each probe is known, and since the deposition location of each probe is known, it is not necessary that each probe comprises a different label. Rather, all that is required is that the site at which each probe is deposited be monitored for tracking. This, in turn, allows each probe to be labeled with the same reporter. (Applicant's specification, at page 14, lines 17-25).

In light of the foregoing, Applicant respectfully submits that Jahn and Schermer could not have made claim 1 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Claims 1, 3, 7, 9, 11-14, 17-18 and 22-28 depend from claim 1 and cannot be made obvious for at least the same reasons as claim 1. Withdrawal of this rejection is thus respectfully requested.

Claim 53, as amended, requires a similar limitation, which is that a plurality of labeled probes are applied to dots individually in the microarray. Therefore, the combination of Jahn and Schermer could not have made claim 53 obvious for the same reasons discussed above. Claims 55-58, 62, and 66-71 depend from claim 53 and cannot be made obvious for at least the same reasons as claim 53. Withdrawal of these rejections is thus respectfully requested.

Claims 1, 7, 8, 10, 13, 14, 17, 18, 21-24, 26, 28, 30, 37-40, 44-47, 49, 53, 55-57, 62, 66-68, and 70 stand rejected under 35 U.S.C. §103(a) as being obvious over Shuber et al., *Human Molecular Genetics* (1997), Vol. 6(3), pages 337-347 ("Shuber") in view of Schermer. The Applicant respectfully traverses this rejection.

Shuber, similar to Jahn, fails to teach or suggest preparing a microarray of any sort, much less a microarray, wherein a probe is applied to dots individually in the microarray.

As discussed above, claims 1 and 53 were amended to recite that the probe is applied to individual dots in the microarray. Independent claim 30 was similarly amended to recite that a labeled nucleic acid probe is applied to dots individually in the microarray.

Shuber teaches blotting amplified DNA samples, each positive for one of 106 mutations, on a membrane. Shuber utilizes a conventional 96-well dot-blot apparatus and applies 30 μl of sample solution to each well. (Shuber, Figure 3 legend and page 345, column 1 under Dot-blots). A typical size of dots obtained with a 96-well apparatus of the type used by Shuber is a few millimeters in diameter (see, for example, attachment in the Applicant's response of April 23, 2003 to the Office Action dated January 23, 2003). Accordingly, Shuber does not teach or suggest applying a probe biopolymer to dots individually in a microarray.

In light of the foregoing, Applicant respectfully submits that Shuber and Schermer could not have rendered obvious claims 1, 30, and 53, because the combination of references fails to teach or suggest each and every claim limitation. Claims 7, 8, 10, 13-14, 17-18, 21-24, 26, 28, 37-40, 44-47, 49, 55-57, 62, 66-68, and 70 depend from either claim 1, 30, or 53 and therefore, cannot be rendered obvious for at least the same reasons as claims 1, 30, and 53. Withdrawal of these rejections is thus respectfully requested.

Claims 1-19, 21-24, 26, 28, 30, 37-40, 44-47, 49, 53, 55-57, 62, 66-68, and 70 stand rejected under 35 U.S.C. §103(a) as being obvious over Shuber in view of Schermer further in view of Balch et al. (U.S. Patent No. 6,312,960 B1) ("Balch"). The Applicant respectfully traverses this rejection.

The above claims consist of either independent claims 1, 30, and 53 or claims which depend from them. Consequently, these claims cannot be rendered obvious over Shuber and Schermer for at least the same reasons as discussed above. Balch cannot remedy the defect of Shuber and Schermer and is not relied upon by the Examiner for such. Instead, the Examiner cites Balch for teaching features of conventional probe arrays and methods of their making. (Balch, column 4, lines 17-41). Balch neither teaches nor suggests anything related to sample arrays, much less methods of preparing a microarray, wherein a probe is applied to dots individually in the microarray.

In light of the foregoing, Applicant respectfully submits that the cited references could not have made claims 1-19, 21-24, 26, 28, 30, 37-40, 44-47, 49, 53, 55-57, 62, 66-68, and 70 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Withdrawal of this rejection is thus respectfully requested.

Claims 1-72 stand rejected under 35 U.S.C. §103(a) as being obvious over Shuber in view of Schermer further in view of Balch further in view of Sirvio et al. (U.S. Patent No. 5,532,311) ("Sirvio"). This rejection is moot with respect to claim 33 due to the Applicant's previous cancellation of this claim in the Applicant's response of April 23, 2003 to the Office Action dated January 23, 2003. With respect to claims 1-32 and 34-72, this rejection is respectfully traversed.

Independent claims 1, 30, and 53 and their dependent claims 2-29, 31, 32, 34-52, and 54-72 are patentable over Shuber, Schermer, and Balch for at least the same reasons discussed above. Sirvio cannot remedy the defect of Shuber, Schermer and Balch and is not relied upon by the Examiner for such. Instead, the Examiner cites Sirvio for teaching a substrate being wetted with an organic modifier selected from dextran sulfate or polyacrylic acid. Sirvio provides a general teaching of processes for modifying surfaces. However, Sirvio has no teaching or suggestion whatsoever of methods of making microarrays, much less of methods of preparing sample microarrays, wherein a probe is applied to individual dots in the microarray.

In light of the foregoing, Applicant respectfully submits that the cited references could not have made claims 1-32 and 34-72 obvious, because the combination of references fails to teach or suggest each and every claim limitation. Withdrawal of this rejection is thus respectfully requested.

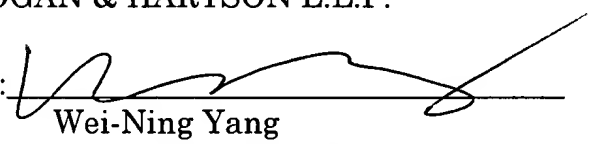
In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6700 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,
HOGAN & HARTSON L.L.P.

Dated: April 6, 2004

By: 
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